

## Neonatal behaviour after drug dependent pregnancy

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**SUMMARY** Neurobehavioural development of 35 infants of drug dependent mothers was compared with the development of 37 reference infants as part of a prospective longitudinal research project. Infants of drug dependent mothers had more poor responses than the other children on neurological examination. This difference is significant only when data of infants of drug dependent mothers born at full term are analysed. Two tailed testing indicated that significantly more infants of drug dependent mothers than reference children had electroencephalograms rated as suspect or abnormal. By the end of the first month the infants of drug dependent mothers tended to be more active, and they had worse scores than the reference children on the neonatal behavioural assessment scale. Analysing data only of infants born at full term, the groups differ significantly on the interactive items. The results of this study show that even after treatment for the neonatal abstinence syndrome, infants of drug dependent mothers seem to differ from comparison children, which could indicate later developmental problems.

Infants of drug dependent mothers are at risk of developmental problems because of exposure in utero to hard drugs. Infants of mothers who used heroin often have lower birth weights than normal control children and the same applies, although to a lesser degree, to infants of mothers who used methadone.<sup>1</sup>

In addition, between 60 and 95% of infants of drug dependent mothers have withdrawal symptoms that can occur up to about two weeks after birth.<sup>2</sup> The symptoms that form the neonatal abstinence syndrome are: symptoms of central nervous system irritability, gastrointestinal problems, respiratory problems, and symptoms affecting the autonomic nervous system.<sup>3</sup> Treatment for the neonatal abstinence syndrome can last from a few days up to several weeks, depending on the severity of the symptoms.<sup>4</sup> Withdrawal symptoms can recur with somewhat lesser intensity over the first six months.<sup>2</sup> Electrophysiological tests have shown low arousal for visual stimulation, and sleep disturbances, in babies of mothers addicted to heroin and methadone.<sup>5</sup>

Infants of drug dependent mothers also seem to differ in behaviour from normal control children during the neonatal period.<sup>6</sup> They seem to be less alert, less cuddly, and less able to respond to visual and auditory stimuli.<sup>5,7</sup> They are also hyperactive,

have extreme fluctuations of muscle tone, their motor responses are less mature, and they show more changes in behavioural states.<sup>8</sup>

Another factor threatening the prenatal as well as postnatal development of the children is the difficult life style of addicts—for example, heavy smoking, poor diet, and often the committing of illegal activities to get money.

Whether these risk factors—drug exposure during pregnancy, neonatal withdrawal problems of the infants, and specific life style of the mothers—have long term consequences on the development of these children is still unknown. In order to study long term development of infants of drug dependent mothers and to find out if they need special intervention or support, a prospective, multidisciplinary, longitudinal research project was started. The design of this study was aimed at detection of medium to large effects.<sup>9</sup> The children were examined from birth to 6 years on physical, neurological, behavioural, and socioemotional scales.

### Subjects and methods

A total of 72 children and their parents were enrolled in the study. The group of infants of drug dependent mothers comprised 35 children. Every drug dependent woman who gave birth in this

hospital from June 1983 to July 1985 was asked to cooperate; only three refused. The mothers had been using street drugs like heroin and cocaine, and were either already using methadone, or had started a methadone maintenance programme when they had discovered their pregnancy. The methadone dose ranged from 5–80 mg/day, and about half used more than 30 mg/day. The drugs were used in various ways, six of the women having it intravenously. As well as using hard drugs, all the mothers in the study group had smoked cigarettes during pregnancy: about half smoked more than one pack daily, about a third smoked half to one pack daily, and about a quarter smoked four to 12 cigarettes daily. Information about the drugs used was obtained by structured interviews and checked against urine analysis, when available. The drugs used are summarised in table 1. All information is presented separately for the total group of full term and premature infants of drug dependent mothers, and for the subgroup of infants born at full term to drug dependent mothers.

Nine infants in the study group were born

preterm: five at 36 weeks' gestation, three at 35 weeks' gestation, and one at 32 weeks' gestation. Twenty nine infants of drug dependent mothers were born spontaneously with cephalic presentation; one child was born by vacuum extraction, one by forceps extraction, two were delivered by caesarean section, and two were vaginal breech deliveries.

A group of 37 infants whose mothers did not use drugs during pregnancy served as a reference group. All the children in this group were born spontaneously with cephalic presentation and at full term. They did not have any serious health problems during the neonatal period.

The infants of both groups were singletons and had no congenital abnormalities. Various characteristics of the infants of drug dependent mothers and reference children are shown in table 2. All the infants of drug dependent mothers, except two showed symptoms of the neonatal abstinence syndrome. Twenty eight children (80%) needed treatment with phenobarbitone for periods varying from eight to 56 days (median 19), three needed treatment for more than 30 days. None of the infants of drug dependent mothers had any serious physical problems other than the neonatal abstinence syndrome during the neonatal period. The infants stayed in hospital from seven to 58 days, mean (SD) 26 (11.4) days. Two were discharged from the hospital to a children's home and one to foster parents.

In general, the social circumstances of addicts are characterised by many problems varying from financial difficulties to legal problems and troubled relations with family and friends. This social background seems to be specific to addicts, and hence a useful comparison with that of other people is hard to make. Looking at several frequently studied

Table 1 *Combinations of drugs used and number of users*

<i>Combinations of drugs used</i>	<i>All drug dependent mothers (n=35)</i>	<i>Drug dependent mothers whose babies were born at full term (n=26)</i>
Methadone	2	2
Methadone and heroin	11	9
Methadone, heroin, and cocaine	16	11
Methadone, heroin, cocaine, tranquillisers, and amphetamines	6	4

Table 2 *Characteristics of the children*

	<i>Reference infants (n=37)</i>	<i>All infants born to drug dependent mothers (n=35)</i>	<i>Infants born at full term to drug dependent mothers (n=26)</i>
Mean (SD) gestational age (weeks)	39.7 (1.0)	38.0 (2.2)	39.0 (1.5)
Mean (SD) birth weight (g)	3428.8 (439.9)	2880.8 (415.3)	3018.0 (365.7)
Birthweight <2.3% growth curve	0	4	4
Apgar score at 1 minute <7	2	4	4
Apgar score at 5 minutes <7	0	1	1
No of girls	20	18	11
No of boys	17	17	15
No of non-white children	15	16	14
No of white children	22	19	12
Mean age of mothers (years)	28.2	27.4	26.7
No of teenage mothers	0	1	1
No of single parents	7	8	8

socioeconomic variables, however, in the reference group, 81% of the mothers were living with a husband or a regular partner, compared with 72% in the study group. In the reference group 32% of the mothers had a job, as did 88% of the fathers, compared with 6% and 19%, respectively, in the study group. Whereas only 28% of the parents in the reference group had to live on a minimum allowance, the percentage in the study group was 90. Secondary education had been completed by 76% of the mothers in the reference group and 71% of the drug dependent mothers.

The examinations started in the first week of life for the reference children, and for those in the study group after treatment of the neonatal abstinence syndrome or (in case of premature babies) at the expected time of birth. All examinations of the preterm children were done at the corrected age. For some of the infants of drug dependent mothers not all the measurements could be done because of the length of time for which they were being treated. Table 3 shows the examinations carried out and the number and mean age of each group at the time of examination.

The neurological examination described by Dubowitz and Dubowitz comprises a number of neuro-behavioural items, and items to judge habituation, movement, and tone as well as some reflexes of the infant; with every item the behavioural state of the infant is also recorded (from 1, deep sleep, to 6, crying).<sup>10</sup> In order to differentiate the groups not only by clinically important signs but also by potentially less remarkable differences, obvious poor responses as well as an optimum category (based on examples from Prechtl<sup>11</sup> and Touwen *et al*<sup>12</sup>) were selected for each item. The mean deviation from the optimum categories was compared for each of the four sections of the scale, as well as for the total scale. As a second measure the number of poor responses was taken. The results of both groups on the 'poor responses' score and the predominant behavioural state of the children during the examination have also been compared. Electroencephalographic output was rated on a scale 1-4 (table 4).

The neonatal behavioural assessment scale<sup>6</sup> illustrates several aspects of the behaviour of infants: interactive responses (like orientation capabilities),

Table 3 Examinations carried out, and number and mean ages of infants examined

Examination	Gestational age at which examination should have been carried out (weeks)	Reference infants		All infants born to drug dependent mothers		Infants born at full term to drug dependent mothers	
		No	Mean age (weeks)	No	Mean age (weeks)	No	Mean age (weeks)
Dubowitz <sup>10</sup>	40	36	40.5	29	40.7	22	41.4
Electroencephalogram	40	35	41.7	32	41.2	25	40.6
Neonatal behavioural assessment scale	40	37	40.2	28	40.3	20	40.8
Activity assessment	40	37	40.2	27	40.3	19	40.7
Neonatal behavioural assessment scale	44	37	43.8	28	44.1	22	44.0
Activity assessment	44	37	43.8	31	44.6	25	44.6

Table 4 Scores on electroencephalography for each group

Score	Reference infants (n=35)	All infants born to drug dependent mothers* (n=32)	Infants born at full term to drug dependent mothers† (n=25)
1 Normal	26	16	12
2 Borderline—a diffuse, somewhat irregular, and little developed pattern	7	6	4
3 Suspect—a diffuse, slow, and irregular pattern with some asymmetry	1	7	6
4 Abnormal—a diffuse, slow, and irregular pattern with focal or paroxysmal aspects or clear asymmetry, or both	1	3	3

\*p=0.006, and †p=0.003 compared with reference infants.

motor responses, behavioural state control, and physiological reactions to stress.<sup>13</sup> In this scale too, one of the rating possibilities for each item has been selected as the optimum category (based on Als *et al.*,<sup>13</sup> and Lester *et al.*<sup>14</sup>), and the mean deviation from the optimum has been compared for each dimension, as well as for the total scale. The predominant behavioural state of the children during the examination has also been compared. The activity, or mobility, of the infants was observed during their baths. Gross motor movements were rated on a seven point scale from 1 (hypoactive) to 7 (hyperactive).<sup>15</sup> Judgments were made over five naturally occurring periods: undressing, soaping, in the bath, drying, and dressing. The mean total score was used for analysis. Interobserver agreement for these examinations varied between 80–91%.

## Results

Nonparametric statistical tests were used because of the ordinal character of most of the results: for all

analyses the Kruskal-Wallis analysis of variance has been calculated, except for the analysis of the electroencephalography results for which Fisher's exact probability test was used.<sup>16</sup> The study aimed to detect medium or large differences between the groups. Two tailed probabilities of at least 0.15 are discussed; a level of significance of 0.05 is accepted, together with a power of at least 0.80.<sup>9</sup>

The results of the neurological examination presented in table 5 show a difference in predominant state during the examination between the groups ( $p=0.005$ ); the infants of drug dependent mothers were more aroused. In addition the infants of drug dependent mothers had more poor responses than the reference children ( $p=0.06$ ). When only the data about the infants born at full term to drug dependent mothers were analysed, the groups differ also on the predominant state during the examination ( $p=0.01$ ) and even more clearly in the number of poor responses ( $p=0.02$ ).

There are significant differences among the groups when electroencephalography results are

Table 5 Results of the neurological examination

	Reference infants (n=36)	All infants born to drug dependent mothers (n=29)	Infants born at full term to drug dependent mothers (n=22)
	Median score (range)	Median score (range)	Median score (range)
Habitual responses*	0.75 (0–2.0)	0.75 (0.20)	0.75 (0–2.0)
Motor responses*	0.88 (0.56–1.69)	0.94 (0.38–1.69)	0.94 (0.38–1.69)
Reflexes*	0.67 (0–1.83)	0.67 (0–1.50)	0.67 (0–1.50)
Neurobehaviour*	1.56 (0.78–2.56)	1.56 (1.0–2.33)	1.56 (1.11–2.33)
Total scores*	0.94 (0.54–1.72)	1.02 (0.67–1.55)	1.03 (0.67–1.55)
Predominant behavioural state	4.0 (2.5–6.0)	5.0† (2.5–6.0)	5.0† (2.5–6.0)
Poor response	2.0 (0–9.0)	4.0‡ (0–12.0)	4.0§ (1.0–12.0)

\*The median of deviations from the optimum is given—the larger the number, the more the deviations. † $p=0.005$ , ‡ $p=0.01$ , § $p=0.06$ , and § $p=0.02$  compared with reference infants.

Table 6 Results of neonatal behavioural assessment scale at the age of 44 weeks

	Reference infants (n=37)	All infants born to drug dependent mothers (n=28)	Infants born at full term to drug dependent mothers (n=22)
	Median (range)	Median (range)	Median (range)
Interactive skills*	2.13 (0.25–4.75)	2.19 (0.71–5.25)	2.25† (0.71–5.25)
Motor skills*	1.83 (0.33–4.50)	2.17 (0.67–3.17)	2.1 (0.67–3.17)
Behavioural state control	1.13 (0–3.86)	1.0 (0.2–4.40)	1.05 (0.20–3.17)
Physical reactions*	0.33 (0–3.67)	1.0 (0–5.0)	0.67 (0–4.0)
Total*	1.36 (0.59–3.36)	1.56 (0.68–3.40)	1.56 (0.68–3.40)
Predominant behavioural state	4.5 (4.0–5.50)	4.50 (4.0–5.50)	4.50 (4.0–5.50)

\*Median=median of deviations from optimal score.

† $p=0.04$  compared with reference infants; none of the other differences is significant.

considered ( $p=0.006$ ) (table 4). The groups also differ when data about the infants born at full term are analysed separately. ( $p=0.003$ ).

On the first neonatal behavioural assessment scale the infants of drug dependent mothers (median=2.33; range=0.33–3.83) tended to have worse scores ( $p=0.14$ ) for the motor responses than the reference group (median=2.00; range=0.33–3.83). At the second examination the groups also tended to differ ( $p=0.09$ ), specifically for the interactive ( $p=0.06$ ) and motor responses ( $p=0.10$ ) (table 6). When the preterm infants of drug dependent mothers are left out of the analysis, a significant difference appears on the interactive responses in the second neonatal behavioural assessment scale ( $p=0.04$ ). In this analysis the groups also differed on the total score ( $p=0.12$ ) and the motor responses ( $p=0.12$ ); neither difference was significant. No significant differences are found on the first observation of the activity of the infants; at the second examination the total group of infants of drug dependent mothers (median=3.20; range=1.60–5.00) tended to be more active than the reference group (median=3.00; range=2.00–5.00;  $p=0.12$ ).

## Discussion

The results show some differences in the neonatal period between the infants of drug dependent mothers and the reference children. More infants of drug dependent mothers had electroencephalograms rated as suspect or abnormal than did reference children. In addition the infants of drug dependent mothers had more aroused behavioural states as assessed by the neurological examination of Dubowitz and Dubowitz.<sup>10</sup> They also had more poor responses on the neurological examination which particularly reflected that they had jerky movements, were easily excitable, quickly became irritated; these aspects of behaviour have been described as indications of drug withdrawal. The analysis of deviation from optimum categories did not show more subtle differences among the children.

Clusters of abnormal signs on neonatal neurological examinations may be indicators of later developmental problems<sup>17</sup> but neonatal neurological examinations are also known for their high rates of 'false positives', although it is still unclear which processes are involved.<sup>18</sup> Possibly the nervous system develops compensatory mechanisms, or signs of dysfunction are not detectable by the time of follow up.<sup>19</sup> With infants of drug dependent mothers, results of a neonatal examination could only indicate temporary dysfunction because of the withdrawal period the children have to go through. Although the children did not need treatment any more by the

time they were examined, the influence of the neonatal abstinence syndrome is suggested by the kind of poor responses they showed, and by the fact that there was a significant difference in the number of poor responses in the neurological examination when the preterm infants of drug dependent mothers were excluded. Due to the age adjustment for these preterm infants, in general treatment for neonatal abstinence syndrome was completed longer before the examination than for the infants who were born at full term to drug dependent mothers.

The results of the observations of activity of the infants and the examinations with the neonatal behavioural assessment scale<sup>6</sup> indicate that the groups might differ by the end of the neonatal period. When only data of infants born at full term are analysed, the interaction items of the second neonatal behavioural assessment scale show a clearer difference, which means that these infants are less clearly responding to their environment. These results suggest differences in the development of both groups during the neonatal period, which could have been influenced both by the drug exposure and the neonatal abstinence syndrome of the infants of drug dependent mothers, and also by their prolonged stay in the hospital resulting in different experiences when compared with the reference group. As well as the analyses presented, the results of the group of infants of drug dependent mothers—with the infants who experienced birth complications excluded—were also analysed. In this way nearly the same  $p$  values were found as in the analysis for the total group of infants of drug dependent mothers.

Contrary to the research of others<sup>5 7 8</sup> no differences were found with the first neonatal behavioural assessment scale. One reason is that the examinations were started when the infants of drug dependent mothers no longer needed drugs which implies that they had already gone through the most serious phase of withdrawal when they were examined. Another reason could be the age difference at the time of examination. In most research with the neonatal behavioural assessment scale, infants of drug dependent mothers are examined and compared in the first week of life.

In this study the groups did not differ in gestational age (table 3) at the neonatal examinations, despite the treatment period that most of the infants of drug dependent mothers needed. Nevertheless, because the infants of drug dependent mothers had a shorter mean gestational period they were somewhat older than the reference group, when age since birth was considered.

A further possible reason for inconsistent findings in different studies of infants of drug dependent

mothers is the variations in drugs used. Possibly differences in kind, combination, quantity, quality, and way the drugs are used exist. For instance, some women inject themselves with a mixture of heroin and cocaine; others use both, but one at a time. Drug abuse can depend on environmental factors—for example, socioeconomic class or habits in the 'drugs-scene'. In addition the metabolism of mother and fetus can influence the effect of the drugs. Probably other confounding variables exist, depending on the life style of the addicts, that may influence the development of the fetus and the postnatal development of the infants. This study shows some differences in the functioning of infants of drug dependent mothers and a group of reference infants in the neonatal period. Longer follow up of these children with various measurements will indicate if these differences point to structural developmental problems or are just temporary difficulties mainly resulting from withdrawal problems.

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